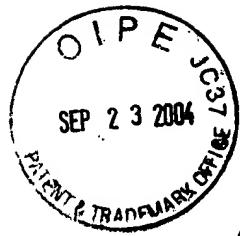


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IN THE UNITED STATES PATENT & TRADEMARK OFFICE

Applicant: Marvin L. Schilling et al

5 Serial No: 09/964,120

Filed: 09-25-2001

For: Method for Producing Biologically Active Products

Group Art Unit: 1616 Examiner: Sharmila S. Gollamudi

10 Hon. Commissioner of Patents

& Trademarks,

Washington, D.C. 20231

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Supplemental Brief under 37 CFR 1.193

Appellants hereby request reinstatement of the appeal as provided for in 37 CFR 1.193 (b) (2) (ii) and file this supplemental brief to respond to the Office Action of 08/05/2004.

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The real parties, the related matters, the status of the claims, the status of the amendments, and summary of invention are the same as set forth in the initial brief.

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As a result of the Office Action the issues in this appeal have changed

dramatically and are as follows.

Group 1

(1) The rejection of claims 42-50 under 35 USC 103(a) as unpatentable over US Patent 5,645,851 to Moore, in view of US patent 4,250,139 to Luck et al and in further view of US Patent 4,404,033 to Steffan et al.

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(2) The rejection of claims 42-50 under 35 USC 103(a) as unpatentable over US Patent 5,645,851 to Moore in view of JP 59025637.

(3) The rejection of claims 33-40 under 35 USC 103(a) as being unpatentable over EP 288405 (abstract) in view of US Patent 5,562,535 to Puppolo. (It is believed that

the Examiner intended to refer to claims 42-50, claims 33-40 are not the claims on appeal, if appellants assumption is in error this issue is moot.

(4) The propriety of the combination references.

5 **Group 2**

(5) The rejection of Claim 51 under 35 USC 103(a) as unpatentable over US Patent 5,645,851 to Moore in view of US patent 4,250,139 to Luck et al in further view of US Patent 4,404,033 to Steffan et al and JP 59-088065.

10 (6) The rejection of Claim 51 under 35 USC 103(a) as unpatentable over US Patent 5,645,851 to Moore in view of JP 59025637 and JP 59-088065.

(7) The rejection of claim 51 0 under 35 USC 103(a) as being unpatentable over EP 288405 (abstract) in view of US Patent 5,562,535 to Puppolo and JP 59-088065.

(8) The propriety of the combination of references.

15 **Grouping of Claims**

The rejections are applicable to all claims in Group 1 and applicable only to claim 51 in Group 2.

(8) **ARGUMENT**

INTRODUCTION

This supplemental brief has become necessary as a result of the examiner for
5 the second time withdrawing a final rejection that forced appellants into the
appeal. Thus the rejections here in issue are based on a third search of the art and
if counting the additional searches conducted during the prosecution, a fifth
search. Both appeal briefs filed earlier apparently were convincing arguments of
the patentability of the claims in issue. The fact that the Examiner required at
10 least three initial searches to find perceived relevant art is of itself evidence of the
fact that the claims are patentable.

Appellants are small entrepreneurs trying to establish a business of preparing
and marketing the product obtained by the process of this invention. In order to
15 protect this business and allow it to survive, appellants require the patent
protection of the claimed invention. The delays that have resulted from the
repeated abortions of the appeals have encouraged competition to their detriment.
The conduct of the Patent Office in this case has been highly prejudicial and
unfair.

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THE INVENTION

The process of the present invention relates to the thermal dehydration of
cartilage that contains Type II collagen, in the presence of an antimicrobial agent and
25 an ionic salt, at temperatures below which denaturization occurs. The denaturization
is defined as any change in the original organic structure of the material being
dehydrated. The dehydration is conducted until the water content is reduced so that it
is no longer subject to pathogenic contamination during a period of commercially
attractive shelf life and is set forth in the claims as below 15 % of the weight of the
30 cartilage. In order to retain the original structure during the dehydration process,
appellants not only use temperatures which are known not to denature the organic
structure of the cartilage, but also employ massive amounts of an ionic salt, which is
combined with the comminuted cartilage itself, in addition to an antimicrobial agent.

The dehydrated product has a salt content of at least 45 %. Because the original structure has been maintained, the benefits from the consumption of the products of the present invention, in relieving the symptoms of rheumatoid arthritis and other diseases, are maximized.

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Claim 43 sets forth the use of the salt in solid form. Claim 44 sets forth a numerical upper temperature limit. Claim 45 further defines the antimicrobial agent. Claim 46 further limits the antimicrobial agent of claim 45 to a hypochlorite. Claim 47 defines the ionizable salt as either potassium or sodium chloride. Claim 48 further defines the salt content of the final product. Claims 49 through 51 incorporate limitations of the earlier dependent claims and further limit the scope of the invention to chicken cartilage.

15 The rejection of claims 42-50 under 35 USC 103(a) as unpatentable over US Patent 5,645,851 to Moore in view of US patent 4,250,139 to Luck et al in further view of US Patent 4,404,033 to Steffan et al.

The Moore reference discloses the thermal dehydration of chicken cartilage and points out that exposing the Type II collagen containing cartilage to boiling water or acid solutions causes the cartilage to become denatured. Moore teaches that it is essential to maintain the insoluble nature of the Type II collagen in order to retain its biological activity and prevent denaturization, which is defined in the patent as the breakdown of the polymeric structure of the Type II collagen causing it to become soluble in water (Column 2, lines 6-19 and column 3, lines 18 –35). In the examples Moore discloses dehydration at 60^0 C (140^0 F) (column 7, line 8), and at an average temperature of 110^0 F, which includes both temperatures above and below 110^0 F (column 7, line 19). Thus Moore contains no suggestion that the drying temperatures used would cause the Type II collagen to denature and suggest to one skilled in the art that the procedures employed in the reference should be modified. There is no appreciation for the specific temperature limit found by appellants to be necessary to prevent denaturing the Type II collagen protein. More importantly there is no suggestion that the drying process should be carried out in the presence of the

substantial quantities of an ionizing salt set forth in the claims to prevent the Type II collagen from denaturing.

The Luck reference relates to the microwave sterilization of proteins without alteration of the physical properties of the protein. A part of that process is dehydration before exposing the protein to the sterilization. The drying employed is lyophilization, thus drying by using reduced pressures to remove the water at very low temperatures. The proteins to be dried are contained in an aqueous mixture. Luck teaches that the drying can be free of salts or salts can be present and if used such salts are adventitiously present in the aqueous phase (column 2, lines 32-49). Thus there is no specific teaching that the presence of salt improves the drying or that the salt should be admixed with the protein. On the contrary the teaching is that the salt is dissolved in the aqueous phase. The insignificance of the salt disclosure is furthermore emphasized by the fact that the reference fails to disclose any salt amounts to be used.

The examiner argues that it would have been obvious to combine the teachings of Moore and Luck and come up with the concept to use salt in the dehydration of Moore' chicken cartilage. The contrary is the case. Nothing in Moore suggests the need for a salt and even less the addition of massive amounts of salt to the cartilage. A person skilled in the art reading Moore would reach the conclusion that adequate drying could be accomplished without the use of a salt. Luck further reinforces that conclusion by teaching that a salt is not needed and that the drying can be adequately accomplished without such salt. In support of such conclusion Luck demonstrates in his examples that lyophilization of proteins is readily accomplished without the addition of salt.

Thus the examiner has relied on the teachings of appellants, on the need of the use of massive amounts of salt in the cartilage, to combine these two references in the attempt to show that feature. In of themselves the references alone or taken in combination do not suggest any improvement in the drying process as a result of using salt. However, even the examiner admits that the references fail to suggest any quantities of salt and that thus the claims distinguish on that basis.

In order to overcome the deficiency of the foregoing combination of references the examiner cites as an additional reference the Steffan patent. Steffan discloses a process for making collagen fibers for surgical purposes. In making such 5 Steffan modifies collagen I containing Achilles tendons chemically by reacting such with an alkali, such as calcium or sodium hydroxide (column 2, lines 46-49). (It is a well-known fact that it is collagen I that occurs in nature in fibular form). Thus the material processed by Steffan is very different from that of Moore or even Luck. It is no longer natural collagen, let alone collagen II. The partial dehydration relied on by 10 the examiner, occurs when the chemically modified collagen is subjected to mechanical pressure such as by passing through fluted rollers. Salt is added in a concentration "between 5 and 15 %" to absorb the water squeezed out by the pressure of the mechanical treatment. At best the salt is used as a desiccant. Furthermore using the standard meaning of "between", the salt concentration disclosed in the 15 reference does not include 15% anymore than the space between two cars includes the two cars. Thus the reference fails to disclose even the lower limit of the salt concentration employed in appellants' process. Reference to the examples (column 5, lines 2-5) further shows that this so-called dehydration process is conducted in the presence of not the salt alone but in the presence of a salt solution.

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More importantly it is apparent that the reference was picked out as a result of computer search with total disregard to the overall teaching in which the computer keywords appear. The reference does not even relate to an edible product, but one that involves reaction with diisocyanates a highly poisonous compound. The section 25 relied on by the Examiner is an intermediate step in a process involving both chemical reaction before the relied on part as well as chemical reaction after the relied on part. Thus before the asserted drying step, the collagen is reacted with alkali, such as sodium hydroxide, over a period of two to five days (column 2, lines 32-49) to change the amide nitrogen content. Obviously this results in the breaking of the protein 30 chains and saponification of the resulting protein molecules. Then the material is treated with hydrochloric acid to neutralize the protein chains and remove non-collagen components such as glycosamines (column 2, lines 50-64). All of this occurs in an aqueous phase, as shown by the examples.

After the dehydration step relied on by the Examiner, the collagen fibers in the resulting aqueous solution are subjected to a crosslinking reaction with a diisocyanate, to further modify the chemical structure of the collagen fiber.

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Clearly there is no intent in the reference to either maintain the original, natural structure of the protein, nor is there an intent to produce a dry product until the described three step process. In addition the dehydration step is at most a mechanical step, which does not remove water to the levels stated in appellants' claims and the

10 Examiner has cited no part of the reference where such is disclosed.

Appellants furthermore traverse this rejection in that the examiner has failed to show any basis or motive for the combination. In their main brief (page 5) appellants have set forth the law applicable to combination of references. The art involved is

15 that of drying collagen II containing natural products while retaining their natural state to preserve the biologically active ingredients of a consumable product. The cited art relates to non-edible surgical fibers that have been reacted with a highly poisonous substance. Why would anyone skilled in the art look at the intermediate step of a chemically modified different collagen that at best employs mechanical

20 dehydration and is not concerned with obtaining a dry product, to modify the drying step that maintains the cartilage with all its organic ingredients and particularly the collagen II in its natural state? There is none. The only connection here is the computer, which of course pays no attention to the context in which the keywords are used.

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Appellants submit that the claims on appeal are patentable over the combination of Moore, Luck and Steffan. None of the references suggests to persons skilled in the art that cartilage and all the ingredients contained in it can be dried to very low water contents using high levels of salt as set forth in appellants' claims.

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Claim 51 has been rejected under 25 USC 103 as being unpatentable
over US patent 5,645,851 to Moore in view of Luck et al US patent 4,250,139
in view of Steffan US patent 4,404,033 in view of JP 59-088065.

Claim 51 is a dependent claim, dependent from claim 49 (there is a typographical error in the numbering, in that it states a dependency on 39, a claim that was cancelled) and claims the dehydration process in the presence of hydroxy-propyl 5 methylcellulose or lecithin. Thus clearly if claim 49 is patentable as argued above, the same would apply to claim 51.

This reference and rejection was argued in the main brief (page 10) in conjunction with another set of primary references and the argument is incorporated 10 herein. The mechanical partial dehydration of the reference fails to suggest the use of lecithin in conjunction with a thermal drying process.

Claims 42-50 have been rejected under 35 USC 103(a) as unpatentable over Moore US 5,645,851 in view of JP 59025637.

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The same rejection was made in the appealed final rejection and is rebutted on pages 8-9 of appellants' earlier brief. In addition it should be pointed out that the reference is a vague abstract without any exemplary disclosure to explain the steps involved. Nothing in the reference suggests that the scallops are to be maintained in 20 their original state. On the contrary the object is to "mature" the mixture, which ordinarily involves some form of oxidation and decomposition, as is pointed out on page 3 of the patent. Furthermore nothing in the reference suggests a specific dehydration. Thus it could involve the use of the salt as just a desiccant, it could involve a partial mechanical dehydration or lyophilization. Nothing in the reference 25 discloses or suggests the degree of dehydration involved in the claims and could involve only the removal of added water as the references using mechanical dehydration suggest. Supporting such is the fact that the reference discloses that the product has a viscous texture suggesting that it is not a dry product but contains significant amount of water. There is nothing in this reference that would suggest to 30 one skilled in the art that the drying process could be improved and the original structure of the cartilage maintained by the addition of large quantities of salt to the cartilage.

The examiner argues that the use of the disclosed amount of salt will result "implicitly" in a salt content of at least 45 % in the dried product. The examiner is wrong since the salt content of the cartilage is also affected by the water content of the cartilage. Thus unless the cartilage is dried to below the 15% water content, the 45 % salt level may not be reached. Since the reference fails to disclose a dry product, the examiner's assertion is speculation.

Again appellants traverse the rejection in that there is no basis or motive for the combination of the reference. What motive would the person skilled in the art to have to look at reference that does not involve the same proteins or similar products, does not disclose a heating process to dry the product and does not disclose a dry product? None!

Claim 51 has been rejected under 35 USC 103(a) as being unpatentable over US Patent 5,645,851 to Moore in view of JP 59 025637 and in view of JP 59-088065.

The same argument as made previously in connection with the Moore and Luck primary references also applies here. Since the primary references fail to suggest the independent claim, dependent claim 51 is patentable over the cited art. Furthermore there is no basis for the combination of the references.

Claims 41-50 (33-40) have been rejected as unpatentable under 35 USC 103(a) over EP 288405(abstract) in view of US patent 5,562,535 to Puppolo. (The copy provided to appellants is a translation of a European French patent application and not just an abstract, although it is believed that that is what the Examiner intends to rely on.)

The Examiner asserts that the reference teaches meat-containing protein. Such characterization of the reference is misleading if not wrong. Basically the reference relates to a process for cooking meat in an autoclave, followed by boiling

the cooked meat to remove water. Thus 67 % of muscle meat, 22% of cartilage and 11 % of fat are placed in an autoclave together with added water (25 % based on solids as exemplified) and 0.1 to 4% of salt, also based on solids. The mixture is then cooked in the autoclave at increasing temperatures from 80 to 130⁰C, for periods of 5 eight to twenty hours. In autoclaving the water is not evaporated but remains as liquid in the meat as a result of the increasing pressure. The cooked meat is cooled resulting in a solution and a solid, which is primarily fat. The water of the solution is removed and then can be dried to form a paste or powder by moderate boiling, atomization or flash drying.

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It is hard to see where this reference has any bearing on the drying process of the appealed claims. Thus there is no intent to make a dried cartilage, which retains its original structure. Autoclaving the meat product at temperatures way above the boiling point of water does not remove water but certainly denatures the protein. It is 15 clear that whatever salt is added, which is far below the concentration of the appealed claims, does not have a stabilizing function in the process. In citing this reference the examiner has totally ignored the teachings of the Moore patent as to the denaturing of the collagen II containing cartilage.

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The secondary reference Puppolo relates to a process for drying shark cartilage to "spare the potential denaturing of its biologically active proteins". The actual process involves as a first step the proteolytic digestion of the shark cartilage to remove the protein. The solution is accomplished by treating the cartilage with a solution of hydrochloric acid or acetic acid also containing a proteolytic enzyme. The 25 proteolytic digestion appears to be squarely contradictory to the stated purpose to spare the denaturing of biologically active proteins. This is then followed by an azeotropic extraction to remove some of the water. Suitable solvents for such azeotropic extraction include benzene, toluene, hexane, and heptane. The remainder of the water, now containing also the organic solvent, is then removed in a sonic drier 30 at temperatures of 85⁰ F.

The examiner attempts to equilibrate the autoclave cooking of the primary reference with the azeotropic distillation of the secondary reference. The two patents

relate to entirely different materials, equipment, processes and purposes without any commonality. The Examiner assumes that the only element missing in the primary reference is the temperature. However the primary reference discloses an operative temperature range, which the examiner appears to ignore in combining the references.

5 Thus the temperatures used in the EP application start at 80° C and increase to above the boiling point of water to as high as 130° C. This corresponds to temperatures of 176° to 266° F which is well known to denature collagen II proteins as set forth in the Moore reference. The examiner cannot ignore these specific teachings of the reference in order to make the reference fit the appealed claims or allow for its combination with other references. Furthermore there is no basis for the examiner to assume that cooking meat in an autoclave process is in any way similar to drying a cartilage in such a way as to maintain the original structure of the collagen II in the cartilage. Although the reference uses salt in the autoclave process it is used in amounts far less than used in appellants claims and furthermore is certainly not used in any drying process since autoclaving the meat prevents the moisture from being removed.

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Appellants further traverse the combination of the references as lacking any basis or motive for their combination. An azeotropic distillation involving an added organic solvent to cause the removal of water has no bearing on cooking meat in a pressurized vessel. They are the opposite since in one the purpose is to remove water and in the other to retain the water. In one reference it is the goal to retain the structure, whereas in the other it is the purpose to denature the meat. Even if the combination is based solely on keywords, even a cursory reading of the references 20 makes clear the diverging subject matter.

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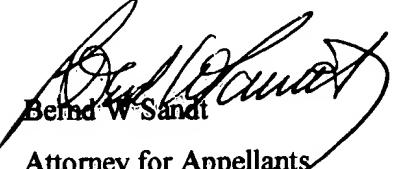
Claim 51 has also been rejected as unpatentable under 35 USC 103 (a) over EP 288405(abstract) in view of US patent 5,562,535 to Puppolo and in view of JP 59-088065.

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Since 51 is dependent from claim 49 it follows that if claim 49 is patentable as argued above so would claim 51. The arguments raised with respect to the third reference in the earlier ejections of claim 51 and especially as set forth in the original

brief at page 11 are equally applicable here. Thus claim 51 is deemed to be patentable.

Appellants submit that rejection of the appealed claims 42-51 continuous to be
5 unjustified and that claims are patentable over the additional art cited by the examiner
as a result of this latest search, and requests that the claims be held allowable.


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20 Certificate under 37 CFR 1.8

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Date: 9/23/04

Signature 